Comments of the

Copper Development Association

on the

Updated Draft of the "Protocol for the Evaluation of Bactericidal Activity of Hard, Non-Porous Copper Containing Surface Products"

For Review by the

FIFRA Scientific Advisory Panel

February 19, 2016

Copper Development Association ("CDA") Comments on the Updated Draft of the "Protocol for the Evaluation of Bactericidal Activity of Hard, Non-Porous Copper Containing Surface Products"

Fundamental technical concerns:

- The Updated Draft Protocol Does NOT Support "Continuous Reduction" Claims: Contrary to the AD's assertion, the updated draft protocol does not support "continuous reduction" claims. As explained in CDA's January 22, 2015, comments, the proposed protocol does not assess efficacy after the types of repeated contamination typical of conditions representative of anticipated use scenarios, and, therefore, does not – indeed, cannot – provide for "continuous reduction" claims. Rather, the proposed protocol only measures performance against a single inoculation of bacteria. While this is a necessary first step in assessing efficacy, testing against a single inoculation says nothing about how the product will perform when faced with the reality of repeated recontamination over time.

  The concept of testing against "repeated re-inoculation" over an extended period of time (not just one hour) to better reflect the real world conditions that these products will encounter (*e.g.*, high touch surface materials) was originated by the AD staff during the 2004-2005 efficacy test protocol development process for solid copper alloy materials. This concept resulted in the development of a protocol ("Test Method for the Continuous Reduction of Bacterial Contamination on Copper Alloy Surfaces") to determine if copper alloy surfaces remain effective after numerous sequential re-inoculations and thereby demonstrate continual antibacterial activity. This test method is far more rigorous than the standard single-inoculation "sanitizer" test that serves as the basis for the new protocol, and is the primary reason why the AD was willing to register copper alloys in 2008.

  Unfortunately, this critical history appears to have been forgotten and the AD now is taking the opposite approach by assuming "continuous reduction" based solely on a single inoculation test for a one-hour period. This is counterintuitive. The AD appears to conflate the evaluation of product durability and performance after being subjected to environmental and chemical stressors as a substitute for establishing "continuous reduction" claims. This approach is incorrect and contrary to a proper efficacy evaluation of these types of products.

  CDA urges the SAP to review the history of the development of the original copper alloy test protocols, particularly the involvement of EPA in developing those protocols, as detailed in CDA's January 22, 2015 comments (attached).

- The Proposed Protocol Should Not Prescribe an Arbitrary "One Hour" Performance Standard; Claims Should Reflect What the Data Show: The specification of a one hour performance time in the proposed protocol is arbitrary. The viability of a particular performance time, and whether a one hour, two hour or other bacteria kill time is meaningful, should be left to the market and consumer choices. In particular, infection control specialists in the healthcare industry are capable of determining if a specific kill time is or is not useful when assessing whether a product makes sense as part of an infection control program. EPA

should not dictate in the proposed protocol a particular time period for performance, but, rather, let the data speak for itself – as the AD determined was appropriate when approving a protocol with a "two hour" contact time in advance of registering copper alloys in 2008. Moreover, specification of a one hour performance time distracts from the primary benefit copper-based products may offer, namely the ability to continuously reduce bacteria levels, as discussed above. The importance of the ability of copper to continuously reduce bacteria levels was demonstrated through clinical trials performed in three hospitals under the auspices of the U.S. Department of Defense ("DoD") which demonstrated that solid copper alloy surfaces reduced the incidence of healthcare associated infections by 58% after the products were subjected to over two years of routine and terminal cleaning with several different EPA-registered disinfectants.[1] The real world clinical setting measured continuous efficacy over 23 months while the laboratory tests (including the proposed one hour test) measure one-time efficacy after a single exposure under ideal laboratory conditions.

Other comments and questions on revisions made to the original draft protocol:

- Page 1, first bullet: The abrasion and chemical exposure period was reduced from twelve weeks to eight weeks. However, the intensity of the exposure testing increased, raising the total number of exposures from 180 to 200. What is the rationale for the proposed exposure timeframe (*e.g.* to simulate X months of surface life)? If the critical requirement is only to reach 200 exposures, could the timeframe be further reduced?

- Page 1, second bullet: If only "unexposed" stainless steel carriers are used for controls, this introduces uncertainty regarding whether or not there are residual antimicrobial or recovery-related effects from the chemical and abrasion treatments. Ideally, both exposed and unexposed stainless steel carriers would be tested.

- Page 3, point 2 under "Product Characterization": The following qualifying statement provides no insight into what information will be suitable for registration purposes: "This information may be documented either as descriptive (qualitative) observations and/or as quantitative measurements."

- Page 3, point 3 under "Product Characterization": The new requirement to describe "distribution of copper in the matrix" provides no clarity on which analytical methods are acceptable.

- Page 4: The time to initiate product performance testing upon completion of the exposure regimen was reduced from two weeks to three days which may introduce significant logistical issues. For example, if a control failure, contamination or other adverse event occurs during the exposure testing, will the entire eight week regimen have to be conducted again from the beginning?

[1] Cassandra D. Salgado, *et. al*., "Copper Surfaces Reduce the Rate of Healthcare-Acquired Infections in the Intensive Care Unit," *Infection Control and Hospital Epidemiology*, vol. 34, no. 5, p. 479-486 (May 2013).

- Page 10, point 12 under "Efficacy Test Procedure": The 1.0 mL option was removed in the revised protocol. The flexibility of using 1.0 mL or 0.1 mL might be necessary in some instances. Likewise, labs may have their own preferences based upon whether they prefer to do spread or pour plating.

- Page 11, point 1 under "Neutralization Confirmation": The revised protocol now requires that neutralization confirmation testing be conducted prior to efficacy evaluation and reported separately. Neutralization control testing should be conducted alongside the test to control for any issues which could occur during the actual test. For example, a technician could forget to rinse a carrier following a final treatment with bleach which could introduce residual antimicrobial activity on that carrier which could overwhelm the neutralizer. This would be missed unless the neutralizer control was run during the test. Furthermore, it is unclear if neutralization confirmation is required only for unexposed test carriers with respect to the chemical and abrasion regimen. If neutralization confirmation is also required for exposed test carriers in advance of the test itself, then more than one exposure cycle would be required if the three day time limit is in place.

* * * *

For additional information or clarification of these comments, please contact Joseph Green, counsel to the Copper Development Association, at 202.342.8849 or JGreen@KelleyDrye.com.